

BEYOND CLEARPET: NEXT AIMS

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ABSTRACT

The CRYSTAL CLEAR collaboration, in short CCC, is a consortium of 12 academic institutions, mainly from Europe, joining efforts in the area of developing instrumentation for nuclear medicine and medical imaging. In the framework of the CCC a high performance small animal PET system, called ClearPET, was developed by using new technologies in electronics and crystals in a phoswich arrangement combining two types of lutetium-based scintillator materials: LSO:Ce and LuYAP:Ce. Our next aim will be the development of hybrid image systems.

Hybrid MR-PET imaging has many unique advantages for brain research. This has sparked a new research line within CCC for the development of novel MR-PET compatible technologies. MRI is not as sensitive as PET but PET has poorer spatial resolution than MRI. Two major advantages of PET are sensitivity and its ability to acquire metabolic information.

To assess these innovations, the development of a 9.4T hybrid animal MR-PET scanner is proposed based on an existing 9.4T MR scanner that will be adapted to enable simultaneous acquisition of MR and PET data using cutting-edge technology for both MR and PET.

Index Terms— hybrid imaging system, small animal MR-PET, monolithic block detectors, depth-of-interaction

1. INTRODUCTION

Considerable progress has been made over the last few years in the development and construction of small animal PET scanners [1,2]. This is mirrored by the fact that after a period of continuous progress within the PET research community industry offers a variety of commercial scanners. These scanners are primarily downscaled from human PET scanners. This refers especially to the size of crystals and the diameter of the detector ring. The kind of detector is, however, unchanged. Especially the readout electronics still employ classical photomultiplier tubes

(PMT). With the development of compact hybrid MR-PET the PMT technology has to be abandoned.

Instead of PMT, which are sensitive to the magnetic fields, solid state photo detectors such as avalanche photo diodes (APD) have been considered [3,4] and inserted into first non-commercial small animal MR-PET prototypes [5]. APD are also used in a first human MR-PET prototype being developed by Siemens [6]. Although the results achieved with the different prototypes are promising it is clear that APD are not optimum as their gain is much smaller than the gain of PMT. Consequently, it is clear already now that additional research is necessary to look for more appropriate solid state readout modules. Silicon PMT (SiPMT), which consist of micro arrays of Geiger-APD are a promising alternative with a much better gain [7], but are not available at high quantities and too expensive.

Animal PET scanners typically have detector rings with small diameters so that their sensitivity is optimized. Detector rings with small diameters are, however, prone to falsely positioned coincidences, which are related to the depth-of-interaction (DOI) problem. As a consequence the transaxial resolution of these scanners decreases rapidly with increasing distance from the scanner's axis. This problem can be reduced by using a double layer of scintillator [8]. On the other hand this solution is also not optimum so that other strategies have to be found to circumvent the DOI problem. Although this problem becomes less important if the crystals are shortened, this easy solution is not desirable because of the loss of sensitivity. Therefore, a new detector concept, which allows simultaneously to yield a better and very uniform spatial resolution and to improve the sensitivity of clinical PET scanner compared to current state of the art systems is needed. To achieve this goal, undivided (or monolithic) scintillator blocks are applied so that there is no efficiency loss due to dead zones in the detector module [9,10]. In addition, the blocks can be made trapezoidal to create a gapless ring and further enhance the detection efficiency significantly. Finally the collection of the scintillation light in monolithic blocks is better than in a matrix of smaller crystals, resulting in an energy resolution of 11% compared

to 20 – 25 % in the classical scanner designs (when using LSO) [11]. With these advantages the novel detector concept is a central issue of the PET-component to be developed for the ultra high-field small animal MR-PET.

2. DESIGN OF MRI COMPATIBLE PET INSERT

The detector modules are based on monolithic scintillator LSO blocks read out by pixelated MRI compatible photo detectors. Using an undivided block of scintillation material increases the detection efficiency significantly. This is due to the absence of dead spaces otherwise introduced by inter-crystal optical separators that are used in the classical designs based on matrices of small individual scintillation crystals.

Upon interaction of an impinging photon in the scintillator, scintillation light is emitted isotropically. However, the 2D light distribution measured by an array of photo sensitive detector elements (Avalanche photo diode array or Silicon PMT array) at the exit surface depends on the position where the photon interacted in the crystal. If the incidence angle is also known (e.g. using the interaction position of the second detected annihilation photon), the interaction position can be related to the incidence position where the photon entered the block. The advantage of acquiring the incidence position is the fact that it is independent of the interaction depth, i.e. there is no problem of parallax errors for oblique incident photons [11].

The incidence position will be extracted from the measured light distribution using neural networks (NN) [12]. Prior to using the neural networks, they need to be trained using a data set with known incidence position and incidence angle for each measured light distribution. These training data sets can be obtained in a first step on a separate bench set-up where a very narrow 511keV photon beam can be positioned at any known position on the scintillator block surface. The final step using a rotational point source inside the scanner plans an in situ calibration. This allows the optimization of the minimal irradiation pattern required to yield accurate position estimates over the complete block surface. Results from laboratory characterization of monolithic blocks using NN algorithms provide intrinsic spatial resolutions below 2 mm (FWHM) [11].

2.1 Monte Carlo simulation

An inevitable step during the design phase of new detectors and detection systems will be the simulation of single components and finally of the complete system. During the approx. 30 years of developing PET it turned out, that simulation studies based on the Monte Carlo technique are the most favorable ones. Similar to the situation in high-energy particle physics, where complex detection systems have to be designed, including the particle tracking and the relative geometrical arrangement this is best solved with

modular program libraries. Such a package of modules is GEANT4, which initially has been developed at CERN (Geneva, Switzerland). In order to ease the application of GEANT4 for simulation of emission tomography devices, the OpenGATE Collaboration has started an initiative to provide a collection of modules suitable to handle specific problems intrinsic to the positron annihilation processes and subsequent detection in various detector arrangements. The GEANT4-based GATE package [13] also includes the application of magnetic fields, a feature, which is important for the simulation of combined MR/PET imaging systems. Specifically the simulation will focus on the following topics to study: arrangement of the individual parts of a detector module, optimization of light collection features of the different crystal sizes and shapes and a detailed study of the accuracy in the determination of the interaction site of the annihilation photon, arrangement of detector modules within the usable field of view (FOV) to optimize both the sensitivity and resolution (but also keeping the costs at a reasonable level), optimization of geometrical data sampling in order to yield best coverage of the imaged volume by the measured coincidence lines of response (LOR). This step will include advanced reconstruction algorithms dedicated to such complex situations.

2.2 Evaluation of silicon PMT arrays

Silicon PMTs (SiPMT) are a novel kind of photo detectors insensitive to magnetic fields [14] that have a number of potential advantages over avalanche photo diodes (APD). The typical gain of SiPMT is 10^5 - 10^6 compared to ~100 for APD and this is achieved at a much reduced working voltage (typically 30V-50V for SiPMT and 350V-450V for APD). However the SiPMT still have a number of parameters, which have to be improved before they can be used as a true alternative to APD. The quantum efficiency (QE) for the detection of LSO scintillation light of SiPMT is lower compared to APD. In addition because of the lower coverage area of the micro amplification channels in the SiPMT “fillfactor”, a non-negligible amount of scintillation light is lost. Finally the dark current, which increases proportionally with the area, is still rather high. Several companies world-wide (e.g. Hamamatsu, SensL, Radiation Monitoring Devices, JINR/Micron enterprise,...) are actively working on producing SiPMT arrays with improved characteristics and the first products are have just appeared on the market. Samples from different companies will be purchased and evaluated by using them to measure light distributions generated in monolithic LSO blocks. A comparison with APD will be done on the basis of

- spatial resolutions obtained after training NNs
- achievable energy resolution
- best possible time resolution

2.3 Front-end and read-out electronics

The geometrical restrictions imposed on a PET ring to be operated as an insert inside a MRI system makes it mandatory to use integrated ASICs for the pre-amplification and amplification of the signals of each detector block. The detector blocks will be based on a 20x20x10 mm LSO crystal that is read out by an 8x8 array of small SiPM pixels. To reduce the number of electronic channels to be read out without losing any positional information, the analog amplifier signals will also be summed in the ASIC. A chip will be designed specifically for such purpose. The chip will deliver the minimum number of outputs needed by the processors to compute the deposited energy, the photon impinging position and a trigger signal.

The analog signals corresponding to the total light deposited by the detector blocks will be digitized by parallel ADCs. The ADCs can be triggered in singles mode (i.e. each detected event is digitized) or in coincidence mode. In the former case a digital time stamp is also produced for each event to allow software coincidence detection. When the system is running in coincidence mode all trigger signals are sent to a coincidence detection unit. Only when two trigger signals from opposing regions of the PET ring are detected within the time window, will the ADCs be triggered. The digital data needs to be transferred to a rack with the data acquisition electronics using optical fibers transmission. To reduce the data size to be transmitted and stored, the digitized data are converted into the incidence coordinates of the photon. This might require an implementation of the trained neural networks in FPGAs for fast real-time conversion.

2.4 Data acquisition and data storage

In order not to repeat the development of a new data acquisition concept, we will apply the philosophy of data acquisition used in the Quick Silver approach used by Siemens [15]. Some small design changes to the Quick Silver architecture will be required to make it compatible with the coincidence unit. According to this philosophy, we increase the degree of compatibility between the MRI platform and the PET ring.

To cope with the expected event rate (singles or coincidences), possible data storage architectures will be explored to select an appropriate one, which can handle the foreseen data rates (up to 2 Mevents/s per block).

2.5 Mechanics

For a modular design, it is desirable for each of the detector modules in the ring to be mechanically independent. A mechanical frame and housing will be designed. Magnetic compatibility is a mandatory issue here. The PET ring to be constructed will be an insert in the MRI scanner. A gantry

encompassing a mechanical support for the module frames, a magnetic field compatible, radio-frequency transparent cover and a mechanical system for translation will be developed.

3. SOFTWARE INTEGRATION

Both imaging techniques have their own acquisition system and dedicated control interface. Nevertheless a common graphical user interface has to be created to take advantage of the combined system. The a priori knowledge of a MRI scan has a potential impact on the PET image reconstruction. At the end MR and PET images are displayed together as a fused image showing the dynamics of tracer uptake in the animal. Furthermore, the combination of structural and functional information can be used for quantitative PET image analysis in animal research studies.

3.1 MR-based attenuation correction

Although the absorption of 511keV photons is much smaller in small animals compared to humans because of the much shorter attenuation paths, accurate quantitative PET imaging depends nevertheless on a satisfying attenuation correction. Combined MR-PET scanners such as the envisaged small animal MR-PET will, however, not contain any facility to measure the tissue attenuation directly as known from standalone PET or PET/CT scanners. In this case, anatomical images provided by the MRI may be used. The aim is to develop a procedure of MRI-based attenuation (MBA) correction. For this purpose appropriate MR images, e.g. T1 weighted ones, will be segmented into compartments which consist of tissue with different attenuation properties. By assigning appropriate attenuation coefficients to the single compartments an attenuation map is obtained. This map will be projected forward into the sinogram space of the virtual scanner, so that the resulting attenuation factors can be used for attenuation correction. The primary issues of this task are to apply or develop a satisfying segmentation of the different tissue compartments and to define their correct attenuation coefficients. The validity of this approach will be checked using phantoms as well as comparative measurements with a Siemens HR+ PET scanner, which offers a transmission scan to get the attenuation map.

3.2 MR-based iterative reconstruction

Due to its limited spatial resolution, reconstructed PET images show a blurring at the border of two tissue compartments in which the radiopharmaceutical is taken up differently. A priori knowledge of the MRI-derived knowledge about the shape of the tissue compartments can be included in a Bayes-based iterative reconstruction procedure [16]. Therefore it is necessary to have a perfect

co-registration between the MR and PET images. This is obviously inherent in a simultaneous MR-PET acquisition so that the need for software-based fusion is obviated. In this task the original MLEM or OSEM reconstruction programs will be modified into maximum a posteriori (MAP) procedures which allow to include the MRI information. Our previous work tested the description of the MRI data via Markov fields and alternatively via Gauss priors. It has to be tested which of these descriptions is optimal in the context of the small animal MR-PET imaging.

3.3 MR-based PET image analysis

Besides the attenuation correction and iterative reconstruction of PET images, quantitative PET image analysis benefits from the complementary structural MRI image information. Depending on the particular animal research study, different volumes of interest (VOI) have to be analyzed with PET. Manual delineation of VOIs in the MRI image is time-consuming and user-dependent. Using semi-automatic and automatic segmentation methods can support this VOI definition yielding more reliable results. Algorithms, developed for human brain segmentation will be adapted for this purpose. Depending on image quality, noise-suppression may be necessary and will be integrated as a pre-processing step. Finally, the segmentation results will be used to account for partial volume effects in PET images based on real shaped 3D structures.

4. SUMMARY AND DISCUSSION

The overall aims are the development and implementation of a hybrid 9.4T MR-PET animal scanner. Much of the necessary work, in the 3-year duration of this application, is to be carried out in a modular way starting with a functioning 9.4T animal MRI scanner based on a clinical software platform. The MRI module, for example, entails the building and testing of parallel transmit and receive RF coils that are PET compatible. Testing of the 9.4T coils for PET compatibility will be carried out in the functioning 3T MR-PET clinical scanner that is at the disposal of the Consortium. Construction of PET detectors that are MRI compatible will proceed in parallel with the MR module in the MRI scanner. Phantom experiments designed to test the performance parameters of each modality will be carried out prior to animal experiments. The work culminates with feasibility studies to demonstrate the advances achievable in MRI methodology and combined MR-PET methodology.

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